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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,504	10/06/2005	Gregory Lee Durst	X16067	4430

25885	7590	01/03/2008
ELI LILLY & COMPANY		
PATENT DIVISION		
P.O. BOX 6288		
INDIANAPOLIS, IN 46206-6288		

EXAMINER	
MABRY, JOHN	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
01/03/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/552,504	DURST ET AL.	
	Examiner	Art Unit	
	John Mabry, PhD	1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,13,38,42 and 48-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,13,38,42 and 48-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/06/07</u> .  | 6) <input type="checkbox"/> Other: _____                          |

***Examiner's Response***

Applicant's response on October 30, 2007 filed in response to the Office Action dated August 16, 2007 has been received and duly noted. In view of this response, the status of the rejection/objections of record are as follows:

***Restriction/Election***

Restriction/Election in the Office Action dated August 16, 2007 is made final. Examiner acknowledges Applicant's withdrawal of their provisional traversal.

***Objection***

The amendment to the bond to the phenyl ring to oxygen being an arrow obviates the objection to formula I in claim 1.

***35 USC § 112***

The 112-2<sup>nd</sup> rejection regarding claims 1, 4-6, 11-30, 42 and 43 regarding the term "CH(OH)C<sub>1</sub>-C<sub>6</sub>alkyl" being indefinite for the carbon being a pentavalent carbon has been overcome in view of Applicant's amendment – deleting the term "CH(OH)C<sub>1</sub>-C<sub>6</sub>alkyl" and inserting the "C(OH)C<sub>1</sub>-C<sub>6</sub>alkyl".

The 112-1<sup>st</sup> rejection regarding claims 42 and 43 of previously examined claims stands rejected. Applicant asserts compounds and compositions of the instant

application are enabled for treatment of benign prostatic hyperplasia (BPH) in a patient. The Applicants shows *in vitro* testing in the form of ER Binding and LNCaP Human PCa Xenograft Assays on page 103, line 19 through page 105, line 12 of the specification. However, there is an *in vivo* test mentioned on page 105, lines 14-32, but there are no test results that indicate treatment of BPH in an animal.

Applicant directs Examiner to US Patent 7,217,734 and corresponding Application Serial No. 10/493,092 and the filed affidavits dated October 27, 2006. However, Applicant does not provide a declaration showing activity of compounds of instant application. The Examiner is not persuaded and respectfully requests parallel *in vitro* and *in vivo* study correlations for compounds of instant application.

Additionally, in response to Examiner's enablement reject (State of the Prior Art) Applicant points out that there are commercially available treatments of BPH. However, as stated by Applicant, commercially available medications such as Cardura, Flomax and Hytrin are alpha adrenergic receptor blockers. In a second group of currently approved medications for treatment of BPH are, for example, Proscar and Avodart which are 5-alpha reductase inhibitors. However, the compounds of the instant application claims to be estrogen receptor beta selective agonist compounds. As far as the Examiner is aware, there are no commercially available medications to treat BPH via 5-alpha reductase inhibition. The current specification would in deed lead to one of ordinary skill in the art to perform undue experimentation for the alleged treatment of BPH of instant application.

**35 USC § 103(a)**

The 103(a) of record has been withdrawn due to Applicant's statement of common ownership in Applicant's Remarks and a new 103(a) is contained below.

***Obviousness-Type Double Patenting***

In response to Office Action dated October 30, 2007, the obviousness-type double patenting rejected has not been overcome over Dodge et al. Examiner is not persuaded by Applicant's arguments of obviousness as mentioned above. Examiner contends that a H of '734 versus  $-\text{CH}_3$  of instant claims are obvious variations of Formula I. Examiner respectfully requests that Applicant submits a terminal disclaimer to overcome this obviousness-type double patenting rejection.

An action on the merits of claims 1, 13, 38, 42, 48, 49 and 50 is contained herein below.

**DETAILED ACTION**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

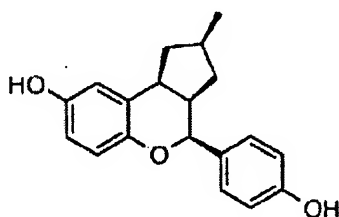
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

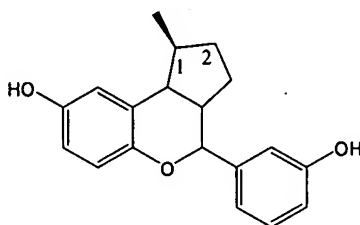
Claims 1, 13, 38, 42, 48, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodge et al (US 6,630,508 B1) in view of Dodge et al (US 7,217,734 B2).

The instant application claims as shown in claim 1, wherein  $G=CH(CH_3)$ .



***Scope & Content of Prior Art MPEP 2141.01***

'508 teaches compounds as described in claim 1, wherein CH<sub>3</sub> group is on the 1 position and an –OH group at the *meta* position on the phenyl ring (see column 2, lines 29-52).



'734 teaches compounds as described in claim 1, wherein –OH group is located at the *para* position on the phenyl ring (see column 2, lines 39-67 through column 3, lines 1-7).

***Differences between Prior Art & the Claims MPEP 2141.02***

'508 differs from instant application at the position of the –methyl group: '508's –CH<sub>3</sub> group at the 1 position versus Applicant's –CH<sub>3</sub> group at the 2 position. These are considered positional isomers.

'734 differs from instant application at the position of the hydroxyl group on the phenyl ring: '734's –OH group at the *meta* position versus Applicant's –OH group at the *para* position. '734 teaches that the –OH group can be placed at the *para* position. These are considered positional isomers.

***Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413***

There is little difference between the methyl being at the 1 position as compared 2 position and the hydroxyl group at the *meta* position compared to the *para* position on the claimed structure instant application. It is well established that position isomers are *prima facie* structurally obvious even in the absence of a teaching to modify. The isomer is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt*, 208 USPQ 343, 349; *In re Mehta*, 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ulliyot*, 103 USPQ 185; *In re Norris*, 84 USPQ 459; *Ex. Parte Naito*, 168 USPQ 437, 439; *Ex parte Allais*, 152 USPQ 66; *In re Wilder*, 166 USPQ 545, 548; *Ex parte Henkel*, 130 USPQ 474; *Ex parte Biel*, 124 USPQ 109; *In re Petrzilka*, 165 USPQ 327; *In re Crownse*, 150 USPQ 554; *In re Fouche*, 169 USPQ 431; *Ex parte Ruddy*, 121 USPQ 427; *In re Wiechert*, 152 USPQ 249, *In re Shetty*, 195 USPQ 753; *In re Jones*, 74 USPQ 152, 154. **There are others as well.** Thus, said claims are rendered obvious by '734.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (*Englehardt*) and "Position isomerism is fact of close structural similarity" (*Mehta*, emphasis in the original). Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent



homologues and structural isomers". Position isomers are the basic form of close "structural isomers." Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds...a known compound may suggest it analog or isomers, either geometric (cis v. trans) or position isomers (e.g. *ortho* v. *para*)." See also MPEP 2144.09, second paragraph. Further, the reference provides for the ring being substituted in any position.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

### ***Double Patenting***

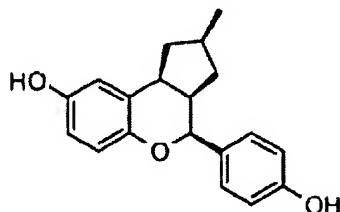
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

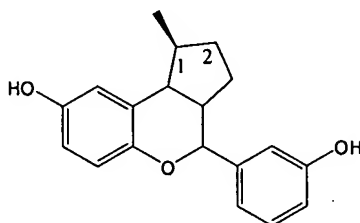
Claims 1, 13, 38, 42, 48, 49 and 50 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Dodge et al (US 6,630,508 B1) in view of Dodge et al (US 7,217,734 B2).

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### **Conclusion**

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

Application/Control Number:  
10/552,504  
Art Unit: 1625

Page 13

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



JM

RITA DESAI  
PRIMARY EXAMINER

  
12/21/07